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# TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Total Number Of Pages In This Submission

Application Number 09/695,807

Filing Date October 23, 2000

First Named Inventor Gregory R. MUNDY, et al.

Group Art Unit 1623

Examiner Name R. Gitomer

Attorney Docket No. 432722002623

## ENCLOSURES (check all that apply)

- |   |  |   |
|---|--|---|
| <input type="checkbox"/> Fee Transmittal Form                                   | <input type="checkbox"/> Assignment Papers<br>(for an Application)                         | <input type="checkbox"/> After Allowance Communication to Group                               |
| <input type="checkbox"/> Fee Attached   | <input type="checkbox"/> Drawing(s)  | <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences           |
| <input checked="" type="checkbox"/> Amendment / Reply                           | <input type="checkbox"/> Licensing-related Papers  | <input type="checkbox"/> Appeal Communication to Group<br>(Appeal Notice, Brief, Reply Brief) |
| <input type="checkbox"/> After Final  | <input type="checkbox"/> Petition  | <input type="checkbox"/> Proprietary Information  |
| <input type="checkbox"/> Affidavits/declarations (see Exhibit A)                | <input type="checkbox"/> Petition to Convert to a Provisional Application                  | <input type="checkbox"/> Status Letter  |
| <input type="checkbox"/> 3 Mos Extension of Time Request                        | <input type="checkbox"/> Power of Attorney, Revocation<br>Change of Correspondence Address | <input checked="" type="checkbox"/> Other Enclosure(s) (please identify below):               |
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| <input type="checkbox"/> Response to Missing Parts<br>under 37 CFR 1.52 or 1.53 |  |   |



25225

PATENT TRADEMARK OFFICE

## SIGNATURE OF APPLICANT, ATTORNEY OR AGENT

Firm or Individual Name	Peng Chen
Signature	
Date	December 17, 2001

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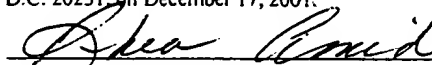
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Gregory R. MUNDY et al.

Serial No.: 09/695,807

Filing Date: October 23, 2000

For: INHIBITORS OF PROTEASOMAL  
ACTIVITY FOR STIMULATING BONE  
AND HAIR GROWTH

Examiner: R. Gitomer

Group Art Unit: 1623

#5  
Jedda  
2/9/02

RESPONSE TO RESTRICTION REQUIREMENT

Assistant Commissioner for Patents  
Washington, D.C. 20231

Dear Sir:

This is in response to the Restriction Requirement mailed November 15, 2001, time for response to which was set to expire December 17, 2001 (December 15, 2001 being a Saturday). A response is timely filed by December 17, 2001 and no fee is due in filing this Response.

IDS

The Examiner states that an IDS was received on July 16, 2001, but no references are found in this file or in 09/421,545.

It is respectfully submitted that Applicants have submitted an IDS and references following a protocol that conforms with 37 C.F.R. §1.98(d) and M.P.E.P. 609(A)(2). Nevertheless, for the Examiner's convenience, Applicants will resubmit all references cited in the 1449 Form via hand delivery in a later date.

#### **Related cases**

The Examiner requested the Applicants to identify all related cases and inform the Examiner how the present application is different from the previous CIP cases.

As disclosed at page 1, lines 3-7 of the present Application, the present application is a continuation-in-part of U.S. Serial No. 09/421,545, filed 20 October 1999, now pending, which is a continuation-in-part of U.S. Serial No. 09/361,775, filed 27 July 1999, now pending, which is a continuation-in-part of U.S. Serial No. 09/113,947, filed 10 July 1998, now pending.

#### 09/113,947

U.S. Serial No. 09/113,947 is directed to methods and pharmaceutical compositions to enhance bone formation, to treat pathological dental conditions, to treat pathological dental conditions, or to treat hair loss using a compound that inhibits the activity of NF- $\kappa$ B or that inhibits proteasomal activity or that inhibits production of these proteins, and methods to identify a compound which enhances bone growth.

The specific compounds that can be used in the treatment methods and pharmaceutical compositions include, though not limited to, lactacystin, a peptidyl epoxy ketone such as EST, MG-132, gliotoxin, MG-115, N-carbobenzoyl-Ile-Glu-(OtBu)-Ala-Leu-CHO (PSI), MG-101 or Calpain Inh I, N-Acetyl-Leu-Leu-Met-CHO (ALLM), N-carbobenzoyl-Gly-Pro-Phe-Leu-CHO, N-carbobenzoyl-Gly-Pro-Ala-Phe-CHO, N-carbobenzoyl-Leu-Leu-Phe-CHO, N-carbobenzoyl-Leu-Ala-Leu-CHO, SN50, Bay 11-7082, Bay 11-7085, Capsaicin, PDTC and MG-341 (*See e.g.*, 09/113,947 at page 24, line 1 through page 26, line 4).

09/361,775

U.S. Serial No. 09/361,775 is directed to methods and pharmaceutical compositions for stimulating hair growth using a compound that inhibits the activity of NF- $\kappa$ B or that inhibits proteasomal activity or that inhibits production of these proteins, and methods to identify a compound which stimulates hair growth.

In addition to the compounds disclosed and/or claimed in 09/113,947, the specific compounds that can be used in the treatment methods and pharmaceutical compositions of 09/361,775 include, though not limited to, Simvastatin, ALLN, MG-262, PPM-18, Cyclosporin A, (*See e.g.*, 09/361,775 at page 13, line 6 through page 15, line 21).

09/421,545

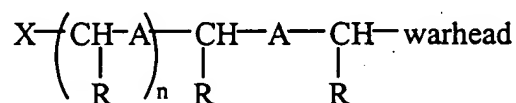
U.S. Serial No. 09/421,545 is directed to methods and pharmaceutical compositions to enhance bone formation or to treat pathological dental conditions or to treat degenerative joint conditions, and methods to identify a compound which enhances bone growth or stimulates hair growth.

In addition to the compounds disclosed and/or claimed in 09/361,775, the specific compounds that can be used in the treatment methods and pharmaceutical compositions of 09/421,545 include, though not limited to, epoxomicin (*See e.g.*, 09/421,545 at page 29, line 1 through page 31, line 29).

The present application (09/695,807)

The present application is directed to methods and pharmaceutical compositions to enhance bone formation or to treat pathological dental conditions or to treat degenerative joint conditions, or to stimulate hair growth using a compound that inhibits the activity of NF- $\kappa$ B or that inhibits proteasomal activity or that inhibits production of these proteins, and methods to identify a compound which enhances bone growth or stimulates hair growth.

In addition to the compounds disclosed and/or claimed in 09/421,545, the specific compounds that can be used in the treatment methods and pharmaceutical compositions of the present application include, though not limited to, a compound that inhibits the chymotrypsin-like activity of the proteasome, *e.g.*, a peptide having at least 3 amino acids and a C-terminal functional group that reacts with the threonine residue of the chymotrypsin-like catalytic site of the proteasome. Exemplary C-terminal functional group include an epoxide, a  $-B(OR)_2$  group, a  $-S(OR)_2$  group and a  $-SOOR$  group, wherein R is H, an alkyl ( $C_{1-6}$ ) or an aryl ( $C_{1-6}$ ). An exemplary epoxide includes an epoxide that forms a morpholino ring with the threonine residue of the chymotrypsin-like catalytic site of the proteasome. Other exemplary compounds that can be used in the treatment methods and pharmaceutical compositions of the present application include a peptide  $\alpha'$ ,  $\beta'$ -epoxyketone, PS-341, NLVS, PSI epoxide, and a compound having the following formula:



wherein the warhead reacts irreversibly with the catalytic chymotrypsin site of the proteasome;

A is independently CO-NH or isostereomer thereof;

R is independently a hydrocarbyl;

X is a polar group; and

$n = 0-2$ .

(*See e.g.*, the present application at page 29, line 1 through page 33, line 20).

The present application is also related to a co-pending application Serial No. 09/558,973, filed April 25, 2000. Aside from some grammatical and stylistic changes, there are three (3) main differences between these two applications. First, one group of compounds used in the

treatment methods and pharmaceutical compositions are different from the corresponding group of compounds in 09/558,973 (please compare claims 11-13 of the present application to claims 11-12 of 09/558,973). Second, the use of PSI epoxide is explicitly recited in the present application (See claim 18 of the present application). Third, Examples 10-12 and 15-16 are added in the present application.

### **Restriction requirement**

Restriction was required among the following four (4) groups:

- I. Claims 1-24, drawn to a method to enhance bone formation, classified in class 514, subclass 2+;
- II. Claims 25-28, drawn to a method to stimulate hair growth, classified in class 514, subclass 2+;
- III. Claims 29-42, drawn to a composition, classified in class 548, subclass 453+; and
- IV. Claims 43-44, drawn to a method to identify a compound, classified in class 435, subclass 23.

Applicants hereby elect to prosecute the claims of group I, claims 1-24. This election is made without traverse with respect to groups II-III and with traverse with respect to group IV. Reconsideration is requested.

The Examiner is correct that the inventions of group I and group IV have different functions at one level. Group I is directed to a method to enhance bone formation or to treat pathological dental conditions or to treat degenerative joint conditions whereas group IV is directed to a method to identify a compound which enhances bone growth or stimulates hair growth. However, it should be clear that the same search is involved in both cases. The method of enhancing bone formation or growth is based on use of compounds which inhibit the activity or production of NF- $\kappa$ B or that inhibit the activity or production of proteasomes. Claims 43-44, the claims in group IV, are directed to an assay method for finding compounds which have the

required inhibiting effect. *The invention in group IV lies not in the nature of the assays, but in the application of these assays to identify bone growth enhancer or hair growth stimulators.*

Thus, the same patentability considerations are relevant with respect to both groups. In view of this, applicants request that their election of group I be extended to group IV as well.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing **432722002623**. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: December 17, 2001

Respectfully submitted,

By: \_\_\_\_\_

Peng Chen  
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Docket No.: 432722002623	Atty: PENG CHEN <i>ra</i> / (W)
Serial No.: 09/695,807	Filing Date: October 23, 2000
Title: INHIBITORS OF PROTEASOMAL ACTIVITY FOR STIMULATING BONE AND HAIR GROWTH	
Date of Mailing: DECEMBER <u>17</u> , 2001	

**Papers enclosed:**

1. Transmittal -1 page;
2. Response, 6 pages
3. Return Postcard.

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